Replimune Provides RP1 Data Update from its Phase 2 Cohorts in Melanoma and Non-Melanoma Skin Cancer that Strongly Support Replimune's Ongoing Registration-Directed Clinical Trials with RP1

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Multiple Complete Responses Observed in Advanced Cutaneous Squamous Cell Carcinoma

High Rate of Deep Responses in Anti-PD-1 / Anti-CTLA-4 Refractory Melanoma

Announces Intention to Commence Clinical Development in Anti-PD-1 Refractory Non-Small Cell Lung Cancer

WOBURN, Mass., June 03, 2020 (GLOBE NEWSWIRE) -- Replimune Group, Inc. (Nasdaq: REPL), a biotechnology company developing oncolytic immuno-gene therapies derived from its Immulytic™ platform, today announced new interim data presented from the Phase 2 part of its Phase 1/2 clinical trial of RP1 in combination with Opdivo® that continues to provide strong support for its lead indications of cutaneous squamous cell carcinoma (CSCC) and anti-PD-1 refractory melanoma.

"CSCC is a significant commercial opportunity that we believe has the potential to drive substantial value for the company. The number of complete responses (CRs) observed is highly suggestive that our combination approach with RP1 can provide better patient outcomes compared to anti-PD-1 therapy alone, where CRs are infrequent," said Philip Astley-Sparke, CEO of Replimune. "In anti-PD-1 refractory melanoma, we believe we also have a strong efficacy signal and are optimistic that our currently-enrolling 125 patient cohort could generate data to support regulatory approval, pending feedback from the U.S. Food and Drug Administration (FDA) and other regulatory agencies. We are also excited to be moving to evaluate RP1 in anti-PD-1 refractory non-small cell lung cancer (NSCLC), given the large unmet need in this tumor type. We believe we have established clinical proof of principle with RP1 in immune-responsive tumor types and in anti-PD-1 refractory cancers, and now have a solid foundation upon which to establish our product candidates more broadly as the second cornerstone of immuno-oncology."

New interim clinical data in CSCC from the enrolling 30 patient non-melanoma skin cancer cohort evaluating RP1 in combination with Opdivo continues to strongly support the Company's registration-directed clinical trial of RP1 in combination with Libtayo®

Overall, four of seven evaluable patients have ongoing CRs and six of seven have an ongoing CR or partial response (PR) (compared to one out of five patients and two out of five, respectively, as presented at the Society for the Immunotherapy of Cancer meeting in November 2019). The data continues to demonstrate that RP1 in combination with Opdivo is well-tolerated, demonstrates immune activation and continues to drive deep and durable responses in patients with CSCC. Furthermore, the number of CRs observed to date in advanced CSCC patients with aggressive disease treated with RP1 in combination with anti-PD-1 provides clear differentiation versus anti-PD-1 therapy alone, which we believe provides the Company strong validation of its clinical development plan.

"The data in patients with CSCC treated with RP1 in combination with Opdivo has continued to strengthen since it was last presented at the SITC conference in November 2019, with PRs converting to CRs, providing patients with the potential for cure, and with further responses observed, including CRs," said Professor Kevin Harrington, PhD, Professor in Biological Cancer Therapies at The Institute of Cancer Research, London, and Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust in theUK. "RP1 in combination with anti-PD-1 therapy therefore appears to be highly active for the treatment of CSCC, both in patients with advanced loco-regional disease, which is the main cause of death in patients with CSCC, and in patients with distant metastatic disease, with the potential to provide a highly effective new therapeutic option for these patients."

The Company's registration-directed Phase 2 clinical trial (CERPASS) in CSCC is a multi-center, randomized, controlled clinical trial intended to enroll approximately 240 patients. The primary objective is to compare the response rate following treatment with RP1 in combination with Libtayo versus Libtayo alone. Libtayo is an anti-PD-1 therapy developed by Regeneron and Sanofi and was approved by the FDA last year for the treatment of patients with metastatic or locally advanced CSCC who are not candidates for curative surgery or radiation. This clinical trial is being conducted under the Company's collaboration agreement with Regeneron. Multiple clinical trial sites in the United States and Australia are open for enrollment. Additional clinical trial sites in these and other countries will be added, with recruitment expected to take approximately 18 to 24 months.

A clinical trial of single-agent RP1 in organ transplant recipients with CSCC is also open for enrollment. This clinical trial is intended to enroll approximately 30 patients and assess the safety and efficacy of RP1 in liver and kidney transplant recipients with recurrent CSCC. Anti-PD-1 therapy is not indicated for solid organ transplant recipients due to the risk of rejection of the transplanted organ.

New interim clinical data in anti-PD-1 refractory melanoma from the fully accrued 30 patient melanoma cohort testing RP1 in combination with Opdivo continues to strongly support the Company's registrational approach

Overall, 36 melanoma patients have been treated in the Phase 1/2 clinical trial of RP1 in combination with Opdivo, of which there were 6 patients in the Phase 1 expansion cohort and 30 patients in the Phase 2 cohort. Sixteen anti-PD-1 refractory cutaneous melanoma patients have been treated. An additional eight patients with anti-PD-1 naïve cutaneous melanoma and 12 patients with uveal or mucosal melanoma (both anti-PD-1 naïve and refractory) have also been enrolled. Initial results from this immature data set (the final patient was enrolled in January 2020) in the anti-PD-1 refractory cutaneous melanoma patients showed:

- Five patients so far have met the formal criteria for response; four of which had previously failed both anti-PD-1 and anti-CTLA-4 therapies
- Two further patients remain on treatment with the opportunity for response
- The minimum final objective response rate (ORR) for these patients will therefore be 31%

The majority of melanoma patients treated with anti-PD-1 therapy have primary resistance, or acquire resistance to checkpoint blockade drugs following initial response. The clear activity of RP1 in anti-PD-1 refractory patients, including in patients with extensive visceral disease, represents a new potential therapeutic option for these patients. Based on the initial efficacy data with RP1 in melanoma, the Company initiated a registration-directed 125-patient cohort of anti-PD-1 refractory melanoma in the Phase 2 clinical trial of RP1 in combination with Opdivo in the first quarter of 2020. The additional cohort is being enrolled under an expansion of the clinical trial collaboration and Opdivo supply agreement with Bristol Myers Squibb (BMS).

Clinical data from the additional patients with anti-PD-1 naïve cutaneous melanoma, mucosal melanoma and uveal melanoma are also supportive of the clinical activity of RP1 in combination with Opdivo. This includes eight patients with anti-PD-1 naïve cutaneous melanoma, six patients with mucosal melanoma and six patients with uveal melanoma.

- Anti-PD-1 naïve cutaneous melanoma (N=8): Four patients so far have met the formal definition of response with two further patients remaining on treatment with the opportunity for response
- Mucosal melanoma (N=6): Two patients (one anti-PD1 naive, one having had prior anti-PD-1) have met the formal definition of response
- Uveal melanoma (N=6): Two patients with extensive liver disease are responding to treatment, both refractory to combined Opdivo and Yervoy®, one so far having a 27.3% reduction by RECIST criteria uni-dimensional measurement and 61% reduction by WHO criteria bi-dimensional measurement

“Responses to RP1 in combination with Opdivo in patients with difficult to treat melanomas who have failed both anti-PD-1 and anti-CTLA-4 would not have been expected for those receiving a second line of anti-PD1 alone,” said Mark Middleton, Professor of Experimental Cancer Medicine in the Department of Oncology, consultant Medical Oncologist at the Oxford Cancer and Haematology Centre and Head of the Department of Oncology at the University of Oxford. “The clinical activity of RP1 in combination with Opdivo in these patients appears robust, with the overall safety profile suggesting no additional toxicities compared to anti-PD1 therapy alone.”

The data from this clinical update can be found in the presentation linked here.

Based on the emerging data indicating that RP1 can be safely administered to tumors in the lung and that evidence of activity, including in anti-PD1 refractory disease, has been observed in patients with lung metastases of other tumor types, the Company announced its intention to enroll a thirty patient cohort of patients with anti-PD1 refractory NSCLC in the Phase 2 clinical trial of RP1 in combination with Opdivo, subject to approval of a protocol amendment by the regulatory authorities. The Company also announced that it plans to terminate the enrollment of the cohort of patients with metastatic bladder cancer in light of changes to the competitive landscape.

Investor event and webcast information
Replimune will host a virtual investor event today, Wednesday, June 3, 2020 at 8:00 a.m. ET. The webcast and accompanying slides will be available under “Events and Presentations” in the Investors and Media section of the company’s website at www.replimune.com. Alternatively, audience members may listen to the call by dialing (833) 651-0806 from locations in the United States and (918) 922-6072 from outside the United States. The conference ID number is 4268503. An archived webcast recording of the event will be available on the website for approximately 30 days.

About CSCC
CSCC is the second most common form of skin cancer and is estimated to be responsible for at least 7,000 deaths each year in the United States. It currently accounts for approximately 20% of all skin cancers in the United States, with the number of newly diagnosed cases expected to rise annually. When CSCC invades deeper layers of the skin or adjacent tissues, it is categorized as locally advanced. Once it spreads to other distant parts of the body, it is considered metastatic. Libtayo® is the only approved therapy in the United States and Brazil, and conditionally approved therapy in the European Union and Canada, for the treatment of locally advanced or metastatic CSCC.

About Melanoma
Melanoma is a form of skin cancer characterized by the uncontrolled growth of pigment-producing cells (melanocytes) located in the skin. Metastatic melanoma is the deadliest form of the disease and occurs when cancer spreads beyond the surface of the skin to other organs. The incidence of melanoma has been increasing steadily for the last 30 years. In the United States, 91,270 new diagnoses of melanoma and more than 9,320 related deaths are estimated for 2018. Globally, the World Health Organization estimates that by 2035, melanoma incidence will reach 424,102, with 94,308 related deaths. Melanoma is mostly curable when treated in its very early stages; however, survival rates are roughly halved if regional lymph nodes are involved.

About RP1
RP1 is Replimune's lead Immulytic™ product candidate and is based on a proprietary new strain of herpes simplex virus engineered to maximize tumor killing potency, the immunogenicity of tumor cell death and the activation of a systemic anti-tumor immune response.

About Replimune
Replimune Group, Inc., headquartered in Woburn, MA, was founded in 2015 to develop the next generation of oncolytic immuno-gene therapies for the treatment of cancer. Replimune is developing novel, proprietary therapeutics intended to improve the direct cancer-killing effects of selective virus replication and the potency of the immune response to the tumor antigens released. Replimune's Immulytic ™ platform is designed to maximize systemic immune activation, in particular to tumor neoantigens, through robust viral-mediated immunogenic tumor cell killing and the delivery of optimal combinations of immune-activating proteins to the tumor and draining lymph nodes. The approach is expected to be highly synergistic with immune checkpoint blockade and other approaches to cancer treatment. Replimune intends to progress these therapies rapidly through clinical development in combination with other immuno-oncology products with complementary mechanisms of action. For more information, please visit www.replimune.com.

Forward Looking Statements

This press release contains forward looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding our expectations about the advancement of our clinical trials, our plans to initiate new clinical trials, our goals to develop and commercialize our product candidates, our expectations regarding commercialization of our product candidates, our expectations regarding the size of the patient populations for our product candidates if approved for commercial use, patient enrollments in our existing and planned clinical trials and the timing thereof, our expectations with respect to our own in-house manufacturing capabilities, and other statements identified by words such as "could," "expects," "intends," "may," "plans," "potential," "should," "will," "would," or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our ability to generate positive clinical trial results for our product candidates, the costs of operating our in-house manufacturing facility, the timing and scope of regulatory approvals, changes in laws and regulations to which we are subject, competitive pressures, our ability to identify additional product candidates, political and global macro factors including the impact of the coronavirus as a global pandemic and related public health issues and other risks as may be detailed from time to time in our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q and other reports we file with the Securities and Exchange Commission. Our actual results could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.

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